REMARKS

By this amendment, claim 49 is amended and claims 55-60 are added. Claims 49-60 are pending. Amendments are discussed below. No issue of new matter arises.

Rejection under 35 U.S.C. §102

Claims 49-54 were rejected under 35 U.S.C. 102(b) as being allegedly "anticipated by Akerblom 'Human leptin receptor-related protein' (US Patent 5,789,198)." At page 4 of the Office Action, the rejection was explained as follows: "The claims do not define or limit the length of the oligonucleotide and expressly include open 'comprising' language. Therefore, the claims do not exclude additional, unrecited elements such as additional unrecited sequences flanking or contiguous with the recited sequence, SEQ ID NO:2." The claim recited "An antisense oligonucleotide" and therefore would have excluded those longer nucleic acids inappropriate as antisense. However, as suggested by the Examiner, claim 49 is amended using language from the specification at page 3, line 23. New claims 55 through 60 are a parallel claim string finding support in the specification for example at page 3, line 25. No issue of new matter arises. For explanation, while Akerblom may have stated: "essentially the same procedure is used with larger cDNA fragments," (OA at page 4, lines 4 and 3 from bottom) the skilled artisan would not reasonably understand this to imply that "possibly full length antisense sequences may be used." (OA at page 4, lines 3 and 2 from bottom) Applicants respectfully submit that as amended the claims even more clearly do not recite the sequence applied in this rejection. Reconsideration and withdrawal of this objection are respectfully requested.

Rejections under 35 U.S.C. §103

Claims 49-54 were rejected under 35 U.S.C. 103(a) as being allegedly "unpatentable over Akerblom 'Human leptin receptor-related protein' (US Patent 5,789,198) in view of

1. Bennett et al. (1999) *Biochimica Biophysica Acta* 1489:19-30;
2. Vickers et al. (2003) *J Biol. Chem.* 278:7108-7118; and
3. Bennett et al. (US Patent 5,998,148)."

Applicants appreciate the Examiner's comments relating to compact prosecution considering claim 49 as if it recited "consisting of". Applicants respectfully traverse this rejection. The Examiner noted: "The instant rejection is rebuttable by objective evidence of

unexpected properties of SEQ ID NO:2." And acknowledged: "Akerblom does not specifically describe the antisense oligonucleotide "consisting of' SEQ ID NO:2." (Page 6. last 2 lines).

However, the Office Action also stated: "In view of this disclosure one of skill would reasonably have envisioned, by visual inspection or computer aided analysis, the complete list of 15-20-nucleotide antisense oligonucleotides complementary to the sequence shown in Figs. lA and B. This list would necessarily have contained the instantly recited antisense oligonucleotide." (Page 7, lines 8-11). MPEP 2144.08 is cited.

Applicants traverse this rejection on two grounds.

1) First Applicants respectfully submit that no *prima facie* case of obviousness has been established.

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. MPEP §2143.

Clearly, the prior art references cannot be said to teach or suggest all the claim limitations. Accordingly, at least the final requirement stated by the MPEP is not met. Thus no *prima facie* case has been established and in accord with the MPEP at 2144.08 the burden has not shifted to Applicants for rebuttal. Reconsideration and withdrawal of this rejection are respectfully requested.

2) In the interest of compact prosecution, and in response to the Examiner's invitation to provide "objective evidence of unexpected properties of SEQ ID NO:2", Applicants respectfully submit that had a *prima facie* case of obviousness been established rebuttal evidence is present to overcome the *prima facie* case. See, e.g., MPEP 2144.08 IIA.

Applicants respectfully cite the present application at page 26, lines 36-44 teaches:

> Fourteen antisenses specific for OB-RGRP (AS 1 to 14) and two random antisenses (AS 15 and 16) were chosen (see Figure 1), synthesized, and then tested for their ability to inhibit OB-RGRP expression using semiquantitative RT-PCR experiments in HeLa cells expressing OB-RGRP endogenously (Fig. 10). **Only one of these antisenses (AS-14), derived from the untranslated 3' region of the OB-RGRP mRNA, interferes with OB-RGRP expression.** Labeling of this antisense with the Cy3 fluorophore made it possible to show that all of the cells were transfected under our experimental conditions, in our various experiments. [Emphasis added.]

Figure 10c pictorially shows the efficacy apparently specific to AS 14. This is directly at odds with the Office Action which stated at page 7, 2nd paragraph:

> In view of this disclosure taken together with the disclosures of References 1-3, above, one of skill would have had reason to make and test as many antisense oligonucleotides in this list as feasible to identify those having the maximum inhibitory activity against LRRP with the reasonable expectation that the most if not all of the antisense oligonucleotides would inhibit the expression of LRRP to some degree.

Either there is no reasonable expectation or the present application shows unexpected results. In the first instance no *prima facie* case of obviousness has been established and rebuttal by Applicants is unnecessary. In any case, the unexpected results shown and discussed in the present application that efficacy is specific to AS 14 (SEQ ID NO:2) would overcome any *prima facie* case of obviousness had one been established. Reconsideration and withdrawal of this rejection are respectfully requested.

New claims

Claims 55-60 are added. Each is ultimately dependent from claim 49 and therefore are patentable over the prior art for at least the same reasons that claim 49 and claims dependent therefrom are patentable over prior art.

Conclusion

In view of the above amendments and remarks, Applicants respectfully submit that the application is now in condition for allowance and request prompt issuance of a Notice of Allowance. If the Examiner wishes to suggest additional amendment that might put the application in even better condition for allowance he is invited to contact Applicants' representative at the telephone number listed below.

Fees

No fees not otherwise provided for are believed necessitated by the instant response. However, should this be in error, authorization is hereby given to charge Deposit Account no. 18-1982 for any underpayment, or to credit any overpayments.

Respectfully submitted,

/George S. Jones/
George S. Jones, Reg. No. 38,508
Attorney for Applicants

sanofi-aventis U.S. Inc
Patent Department
Route #202-206 / P.O. Box 6800
Bridgewater, NJ 08807-0800
Telephone (908) 231-**3776**
Telefax (908) 231-2626
sanofi-anevtis Docket No. FRAV2003/0005 US NP